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Clinical implications of acetaldehyde adducts with hemoglobin.

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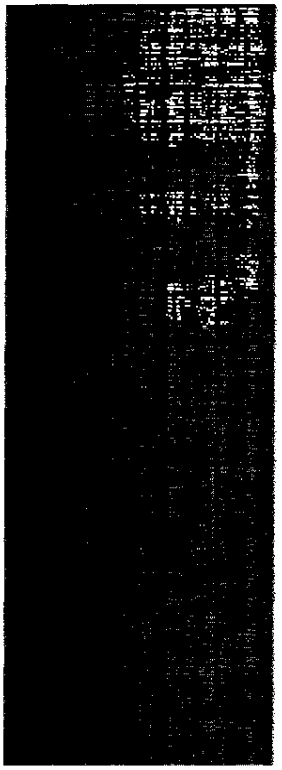
Acetaldehyde has been found to form adducts with human hemoglobin, a portion of which (15-25%) are stable to dialysis. The reaction is nonenzymatic and occurs with purified hemoglobin A. As determined by incorporation of radioactivity, the amount of stable hemoglobin adducts formed is proportional to the amount of acetaldehyde to which hemoglobin is exposed, or to the number of intermittent pulses. Reaction of hemoglobin A with 3 to 30 mM acetaldehyde significantly increases the amount of minor hemoglobins recovered following chromatography on cation exchange resin. Acetaldehyde adducts with hemoglobin involve primarily the beta chain and at least three different amino acid residues (valine, lysine and tyrosine), and two modified residues (glucosyl-valine and glucosyl-lysine). The acetaldehyde appears to be reacting with the epsilon-amino group of lysine and alpha-amino group of valine probably through an initial Schiff's base reaction. The secondary amines of glycosylated valine or glycosylated lysine residues are also proposed to be at the sites of reaction with acetaldehyde. Disubstitution of amino groups is known to occur with hexose sugar (Schwartz, Gray 1977) and by analogy, acetaldehyde might also react with the secondary amine of glycosylated residues. Acetaldehyde adduct formation with tyrosine residues may involve either a nucleophilic attack by the third or fifth carbon of the phenolic ring, analogous to formaldehyde modification of proteins (Blass, Bizzini, Raynaud 1965) or alternatively by reaction with the hydroxyl group of tyrosine. Only a portion of the stable hemoglobin-acetaldehyde adducts which were stable to 24h of dialysis could be irreversibly fixed by sodium borohydride or cyanoborohydride reduction. A greater portion however appeared to be in a non-reducible (non-carbonyl, non-amino) form. Up to 45% of the dialysis stable adducts could be reduced by sodium cyanoborohydride and be hydrolyzed to amino acid adducts if given either sufficient reduction time (2-3 weeks at 22 degrees C) or increased temperature (1-2 days at 50 degrees C). An increase in reducible adduct recovery occurred in all 5 residues detected



by amino acid analysis. This suggests that the adducts that are stable to acid hydrolysis form and reverse through a reducible (e.g. Schiff base) form but that most of the time the adducts occur in a non-reducible state. At present, assay systems are not available which can detect acetaldehyde adducts in the blood of humans consuming alcohol.(ABSTRACT TRUNCATED AT 400 WORDS)

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